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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/874,198 | 06/04/2001 | Jens Chr. Jenscnius | 09011-002002 | 2556 |

1444 7590 04/21/2004

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| EXAMINER | |
|---|---|
| MOORE, WILLIAM W | |
| **ART UNIT** | **PAPER NUMBER** |
| 1652 | |

DATE MAILED: 04/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/874,198 | JENSENIUS ET AL. | |
| | Examiner | Art Unit | |
| | William W. Moore | 1652 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *11 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *4,5,22,28,46,47,49-54 and 57-71* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *4,5,22,28,46,50,54,57-61 and 64* is/are allowed.

6)☒ Claim(s) *47,49,53 and 65-71* is/are rejected.

7)☒ Claim(s) *51,52,62 and 63* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Response to Amendment*

Applicants' amendment filed December 11, 2003, has been entered, inserting sequence identifiers after the descriptions of amino acid sequences at pages 15, 44, and 46-48 of the specification, amending claims 4, 22, 28, 46, 47, and 49-53, adding the new claims 57-71, and canceling claims 6, 11, 41-45, 48, and 55. The claim additions and cancellations submitted December 11, 2003, leave claims 4, 5, 22, 28, 46, 47, 49-54, and 57-71 pending herein. Because the specification discloses that at least one species – the native MASP-2 protease – among the broad genera of claims 47, 70 and 71 has a utility recited by the amended and new claims, all of the pending claims free of the rejection of record herein under 35 U.S.C. § 101. The claim amendments submitted December 11, 2003, also remove claims 4, 5, 22, 28, 46, 50-52, 54, and 57-64 from the rejections of record under 35 U.S.C. § 112, first and second paragraphs. Yet claims 47, 49, 53 and 69-71 remain subject to the rejections of record under 35 U.S.C. § 112, first paragraph, and claims 51, 52, 62, and 63 which depend from these rejected claims are objected to even though the subject matters they describe are free of the rejections of record. It is noted that amending claims 51 and 52 to depend from claim 50, rather than from claim 47, would free claims 51, 52, 62, and 63 from the objection stated below. The new claims 65-68 state the limitation "conservative", which necessitates a new ground of rejection under 35 U.S.C. § 112, second paragraph.

### *Claim Objections*

Claims 50 and 71 are objected to because of the following informalities: Before the second instance of "polypeptide" in claim 50 there is an ungrammatical and superfluous recitation of "the". At the fifth line of the preamble in claim 71 there is an absence of a grammatically necessary conjunction. Appropriate correction of both claims is required.

*Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 47, 49, 53 and 69-71 are for reasons of record rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant's arguments filed December 11, 2003, have been fully considered but they are not persuasive. Applicant suggests at pages 18-19 of the response filed December 11, 2003, that a single disclosed species might be sufficiently representative of undisclosed species that diverge as much as 15% in amino acid sequence identity from that single species. Yet the specification provides no identifying characteristics of any other products that differ in their amino acid sequences and fails to exemplify or describe the preparation of members of this broad genus of polypeptides that exhibit the activities recited in claims 47 and 50 and required in claims 53 and 69 that depend therefrom, or that have the characteristics recited in claims 70 and 71, which require no significant structural similarity to the single disclosed species of MASP-2. The specification cannot identify or suggest acid positions within the amino acid sequence of SEQ ID NO:2 wherein amino acid sequence modifications should be made according to claims 47and 50. Where the artisan reading the specification cannot ascertain the nature of the claimed, but undisclosed, species of claims 47, 49, 53 and 69-71, the artisan could not recognize that Applicant was in possession of these subject matters at the time the specification was filed. "While one does not need to have carried out one's invention before filing a patent application, one does need to be able to describe that invention with particularity" to satisfy the description requirement of the first paragraph

of 35 U.S.C. §112. *Fiers v. Revel v. Sugano*, 25 USPQ2d 1601, 1605 (Fed. Cir. 1993). Nothing demonstrates that, at the time the specification was filed, Applicant was "able to envision" enough of the structure of the undisclosed generic proteins reached by the claims rejected herein to provide the public with identifying "characteristics [that] sufficiently distinguish it . . . from other materials". *Fiers*, 25 USPQ2d at 1604 (citing *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991). The rejection of record is sustained because the specification's treatment of the claimed subject matter is considered to be entirely prospective where skilled artisans in the relevant fields of molecular biology and medicine could not predict the structure, or other properties, of the generic products of claims 47, 49, 53, and 69-71.

Claims 47, 49, 53 and 69-71 are for reasons of record rejected under 35 U.S.C. § 112, first paragraph, because the specification is not enabling for the preparation of a functioning human MASP-2 protease having an amino acid sequence that diverges from the amino acid sequence of SEQ ID NO:2, nor for a product that diverges as much as 15% from the amino acid sequence of SEQ ID NO:1 that has any use in identifying a native, human, MBL-MASP-2 complex. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, make and use the invention commensurate in scope with these claims.

Applicant's arguments filed December 11, 2003, have been fully considered but they are not persuasive. Applicant suggests at pages 23-24 of the response filed December 11, 2003, that methods for permutation of regional amino acid sequences and a method for finding critical residues where alanine substitutions will abolish activity can guide the artisan to both sites and substituents for altering 15%, or 10%, of the amino acid sequence of SEQ ID NO:2 between the positions 17 and 686. The specification already identifies the active site regions, which are reflected in clauses (1) through (4) of claim 71, but fails to identify the great majority of amino acid positions that provide the secondary and tertiary structural features of MASP-2 that permit it to recognize complement and to be influenced by mannan-binding. Mere sequence perturbation cannot enable the design and preparation of a myriad of divergent

proteases that will provide the public with a protease that retains its native functions. The standard set by the CCPA, the precursor of the Court of Appeals for the Federal Circuit, is not to "make and screen" any and all possible alterations because a reasonable correlation must exist between the scope asserted in the claimed subject matter and the scope of guidance the specification provides. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 25 (CCPA 1970). The Federal Circuit approved the CCPA's standard in *Genentech, Inc. v. Novo-Nordisk A/S*, 42 USPQ2d 1001 (Fed. Cir. 1997). Because claims 47, 49, 53 and 69-71 contemplate arbitrary assignments of amino acid substitutions anywhere in the sequence of the disclosed, native, human MASP-2 protease, and because neither the specification nor the prior art of record, taken together, can support the introduction of amino acid substitutions at as many as 100 (15%), or even as few as 67 (10%), of the unspecified amino acid positions within the amino acid sequence region defined claims 47 and 50 – and regions undefined by claims 70 and 71 – yet produce a variant that retains either a native protease or a mannan-binding lectin-associating activity, the rejection of record is sustained.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 65-68 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

This new ground of rejection is necessitated by introduction of the new claims 65-68 which are indefinite because the specification's sole description, at page 11, of amino acid substitutions that are "conservative", indicates "typical" alternatives for 15 of the 20 naturally-occurring amino acids where the use of "typical" fails to provide a measure of similarity with which metes and bounds of the claims can be determined.

*Allowable Subject Matter*

Claims 4, 5, 22, 28, 46, 50, 54, 57-61 and 64 are allowed herewith and claims 51, 52, 62, and 63 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten to include all of the limitations of claim 50, rather than claim 47 from which they currently depend.

*Conclusion*

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is now 571.272.0933. The examiner can normally be reached between 9:00AM and 5:30PM EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can now be reached at 571.272.0928. The fax phone numbers for all communications for the organization where this application or proceeding is assigned remains 703.872.9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is now 571.272.1600.

William W. Moore
April 19, 2004

NASHAAT T. NASHED PHD.
PRIMARY EXAMINER